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10/518,610	06/16/2005	Ghanem Elias Ghanem	27656/40760	3634

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EXAMINER
GUPTA, ANISH

ART UNIT	PAPER NUMBER
1654	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/518,610	GHANEM ET AL.	
	Examiner	Art Unit	
	Anish Gupta	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *07 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,11,16,18 and 20* is/are pending in the application.

4a) Of the above claim(s) *2,6,7 and 18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-5,8,11,16 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2-14-05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed, December 7, 2007 is acknowledged. Claims 1-8, 11, 16, and 18 were amended, claims 9-10, 12-15, 17 and 19 were canceled, and claim 20 was added. Claims 1-8, 11, 16, 18 and 20 are pending in this application.

Election/Restrictions

2. Applicant's election of Group I, claims 1-8, 10, 11, 16, with the elected species of Pro-Phe-p-F-Phe in the reply filed on December 7, 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

A search was conducted for the elected species and it was deemed to be free of the prior art. In accordance with markush practice, the search was extended to the species of the tripeptide Val-Arg-Phe. Claims 1, 3-5, 8, 16 read on the elected specie. Note that clams 2-4, 6-7, 11, and 18 have been withdrawn from consideration because the MPEP states "If prior art is then found that anticipates or renders obvious the Markush-type claim with respect to a nonelected species, the Markush-type claim shall be rejected and claims to the nonelected species held withdrawn from further consideration. The prior art search, however, will not be extended unnecessarily to cover all nonelected species." It should be noted, to further prosecution, the search was extended to the markush type claim 1 with drug being adriamycin. Thus, claims 1, 3-5, 8, 11, 16, 20 have been examined and claims 2, 6-7, and 18 have been withdrawn from consideration.

Claim Objections

3. Claims 1 and 4 are objected to because of the following informalities:

In claim 1 the claims states that the amino acid moiety that is connect to. However the claim should state "connected to."

In claim 4, the claims states that peptide of claim 1 comprising "a not terminally optionally substitute phenylalanyl moiety." However, the claim should be amended to recite the tripeptide of claim 1 wherein the tripeptide does comprise a terminal phenylalanine or a substituted phenylalanine residue. This would make the claim language clearer.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1 and 5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites "pharmacologically active site." It is unclear what moiety or compounds are considered "pharmacologically active site." A pharmacologically active site would normally be defined to be the site of action for the pharmaceutical. Thus, it is unclear if the receptor site, or cell, or any other site where the pharmaceutical is directed to is modified with the peptide.

Claim 5 clams four different tetrapeptides. However, the base claim and claim 5 itself recites only tripeptides. Thus, claim does not further limit the base claim.

In claim 5, the claim recites the peptide pro-phe-phe twice.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1, 3-5, 8, 11, 16, and 20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that

distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP 2163.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In Regents of the University of California v. Eli Lilly & Co., the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials. Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606; In re Smythe, 480 F.2d 1376, 1383, 178 USPQ 279, 284-85 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus. . . ."). Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. The MPEP states that for a genus claim, written description may be satisfied by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.. Further, the MPEP does state that for generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP 2163. Although the MPEP does not define what constitute a sufficient number of representative, the Courts have indicated what do not constitute a representative number species to adequately describe a broad generic. In Gostelli, the Court

determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. In re Gostelli, 872 F.2d at 1012, 10 USPQ2d at 1618.

In the instant case, the claims recite a tripeptide comprising a proteyolytic enzyme cleavable amino acid moiety conjugated to a drug, pharmacologically active site, or pharmacologically active group. The generic statements of a tripeptide comprising a proteyolytic enzyme cleavable amino acid moiety and drug, pharmacologically active site, or pharmacologically active group, does not provide ample written description for the compounds since the claims do not define the requisite relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics. Indeed the base claim does not define a singe structural feature, besides the presence of an amide bond. The mere presence of three amino acids, to form the tripeptide, does not provide ample written guidance since one of ordinary skill in the art cannot determine which naturally or non-naturally amino acids comprise the tripeptide. This is also true of the drug and pharmacologically active site, drug or pharmacologically active group. The claims do not define any identifying characteristics or any structural insight into the said agent, site, or drug.

As stated earlier, the MPEP states that written description for a genus can also achieved by a representative number of species within a broad generic. It is unquestionable claim 1 is a broad generic with respect all possible compounds and peptides encompassed by the claims. The possible structural variations are limitless to any class of drug, active agent, or active site and any tripeptide. The possible number of peptides encompassed by the claims are 2^{20} or 3,486,784,401 different possibilities when only naturally occurring amino acids are used. This does not include those peptides that contain side chain modifications and/or have non-naturally occurring amino

acids. The specification disclose eight tripeptides, FFP, PFF, FFS, SFF, FFN, NFF, FRV, VRF. Most of these peptides contain two Phenylalanine and are retroinverso of their counterpart. These eight tripeptides do not provide a representative number of examples for 3,486,784,401. None encompassed by the claims have modification, aside from the presence of a fluorine on the para position of the Phe residue. None of the peptides disclosed utilize any nonnaturally occurring amino acids such as Norvaline, norleucine etc....

Similarly, the specification does not provide a representative number of examples for the drug, active agent, or active site to which the peptide is connected. The specification only describes these moieites in a generic manner by stating the drug can be a drug for the treatment of arthritis, aids, tumors, and malaria. However, the specification never disclose any specific drug, aside from adriamycin, that is conjugated to the tripeptide. It should be noted that the MPEP states that "a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species" See MPEP 2163. Here, the specification does not even disclose a "laundry list" of drug, active agent, or active site. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 1, 5, 8 and 16 are rejected under 35 U.S.C. 102(e) as being anticipated by Pei et al. (US20040009956).

The claims are drawn to a tripeptide conjugated to an active agent.

The reference disclose a phosphotyrosine mimetic conjugated to the peptide VRF (see claim 13). The peptide Val-Arg-Phe is one of the tripeptides claimed in claim 5. The non-peptide portion of the molecule meets the limitation of the pharmacologically active group.

7. Claims 1, 3-4, 11, and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Bebbington (WO200200263).

The claims are drawn to a tripeptide conjugated to an active agent.

The reference disclose a tripeptide conjugated with doxorubicin. The reference specifically discloses tripeptides such as met-ala-leu and leu-ala-leu conjugated to doxorubicin. Doxorubicin is also known as adriamycin. Thus, the reference meets the limitation of the claims.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anish Gupta whose telephone number is (571)272-0965. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can normally be reached on (571) 272-0562. The fax phone number of this group is (571)-273-8300.

Anish Gupta
Patent Examiner